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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/967,263	09/28/2001	Timothy O'Brien	D6415	5220

7590 08/24/2005

Benjamin Aaron Adler
ADLER & ASSOCIATES
8011 Candle Lane
Houston, TX 77071

EXAMINER	
UNGAR, SUSAN NMN	
ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 08/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/967,263	O'BRIEN ET AL.	
	Examiner	Art Unit	
	Susan Ungar	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *08 July 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1 and 5* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☑ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/5/03*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

S.O.O.

1. The Amendment filed July 8, 2005 in response to the Office Action of February 7, 2005 is acknowledged and has been entered. Previously pending claim 1has been amended. Claims 1 and 5 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The following rejections are being maintained:

Claim Rejections - 35 USC 103

4. Claims 1 and 5 remain rejected under 35 USC 103 for the reasons previously set forth in the Paper mailed February 7, 2005, Section 3, pages 2-9.

Applicant argues that since Examiner rejected Applicant's arguments drawn to the use of HERCEPTIN alone because the claims are not drawn to a method "consisting" of the administration of HERCEPTIN, amendment of claim 1 to substitute the term "consisting" for the term "comprising" overcomes the rejection. The argument has been considered but has not been found persuasive because Examiner specifically stated that the art teaches the successful use of HERCEPTIN alone for the treatment of Her-2/neu overexpressing tumor and given that teaching it would have been *prima facie* obvious to treat any tumor with HERCEPTIN alone or in combination with a chemotherapeutic agent for the reasons of record. Thus, the claimed invention remains obvious in view of the teachings set forth in the Paper mailed February 7, 2005 that a method of treating cancer with HERCEPTIN alone clearly was effective as disclosed by Pegram et al who clearly teach the effectiveness of the antibody alone for *in vivo* treatment. Further, as previously set forth, a method of treating patients with HERCEPTIN alone

was successful for a subset of the cases documented wherein not only partial but also a complete responder was reported and wherein it was found that upon treatment with HERCEPTIN alone, 39% of the patients assessed met the criteria for stable disease as taught by Bookman et al. As set forth previously, "Given this teaching, despite suggested combination of HERCEPTIN with cisplatin, it is clear that one of ordinary skill would have a reasonable expectation of success in treating any cancer that overexpresses HER-2/neu with HERCEPTIN alone" (see page 5 of the previous Action).

Applicant further argues that since Pegram et al and Bookman et al found low response rates for treatment with HERCEPTIN alone, the prior art in combination do not teach or suggest all of the elements of Applicants' amended claim. The argument has been considered but has not been found persuasive as drawn to Pegram et al because, Applicant is misrepresenting the teachings of Pegram et al. As previously set forth, Pegram et al do not teach that treatment with HERCEPTIN alone was not effective, rather Pegram et al teach that response rates of the combination therapy were higher than that of the anti-Her-2/neu monoclonal antibody alone. Further, although Bookmen et al specifically suggest the combination therapy, Bookmen et al also teach the successful use of HERCEPTIN alone for the reasons of record. Applicant further argues that, Bookmen et al explicitly state that based on low frequency of HER-2/neu over-expression and very low response rates to single agent HERCEPTIN, it would be practical to combine HERCEPTIN with platinum based therapy. The argument has been considered but has not been found persuasive because, in particular as drawn to frequency of HER-2/neu over-expression, as previously set forth Berchuk found that 25% of the uterine papillary carcinomas tested had high HER-

2/neu staining, Saffari et al demonstrated that 33% of the uterine papillary carcinomas tested had high HER-2/neu expression and Wang et al teach that a 100% of uterine papillary carcinomas tested presented with high Her-2/neu expression. Given this information, one would have a reasonable expectation that at least a subset of patients with papillary carcinomas would be successfully treated with HERCEPTIN alone, given the high level of expression of Her-2/neu documented in these tumor types.

Although Bookman et al suggest targeting other related signal transduction molecules to increase the proportion of patients that might benefit from combined therapy, given the information known in the art it is clear that one could expect to treat any type of cancer, including papillary carcinomas that overexpress Her-2/neu with HERCEPTIN alone with a reasonable expectation of success. Further, although Applicant suggests that the prior art merely suggests that based on the prior art one would be merely trying to arrive at the claimed invention and that the prior art references combined do not suggest all of the elements of the instant invention, for the reasons set forth previously and above, given the known efficacy of HERCEPTIN alone on Her-2/neu overexpressing tumors, given the known information that at least a subset of papillary carcinomas overexpress Her-2/neu, one would have a reasonable expectation of successfully treating papillary carcinomas with HERCEPTIN alone. The arguments have been considered but have not been found persuasive and the rejection is maintained.

Claim Rejections - 35 USC 112

5. Claims 1 and 5 remain rejected under 35 USC 112, first paragraph for the reasons previously set forth in the Paper mailed February 7, 2005, Section 4, page 9.

Applicant argues that the specification clearly discloses HERCEPTIN to contain human framework regions with complementary-determining regions of a murine antibody that binds to the Mw 185,000 extracellular determinant of HER-4/neu and points to page 18, lines 9-12. Furthermore, based on the amendments to the specification mailed December 11, 2003, HERCEPTIN was described as a humanized murine anti-HER-2/neu monoclonal antibody. Further, this is information well known in the art. Thus, contrary to the Examiner's contention of no support for HERCEPTIN to be a humanized murine monoclonal antibody 4D5, Applicants have shown said support in their own specification in addition to the knowledge common to those of ordinary skill in the art. The argument has been considered but has not been found persuasive because Applicant is arguing limitations not recited in the claims as currently constituted. The claims as currently constituted are not drawn to HERCEPTIN, but rather are broadly drawn to any humanized murine anti-HER2/neu 4D5 monoclonal antibody with alterations in the framework or variable regions that are different from those of HERCEPTIN. The specification as originally filed provides no support for any humanized murine antibody other than HERCEPTIN, does not contemplate the use of any humanized anti-HER2/neu monoclonal antibody other than HERCEPTIN. The amendment to the claims broadened the scope of the invention as originally disclosed in the specification and thus the added claim limitation is new matter. The arguments have been

considered but have not been found persuasive and the rejection is maintained.

6. All other objections and rejections recited in the Paper mailed February 7, 2005 are hereby withdrawn.

7. No claims allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (571) 272-0837. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at 571-272-0787. The fax phone number for this Art Unit is (571) 273-8300.

Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers

for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.

Susan Ungar
Primary Patent Examiner
August 17, 2005